

WS23.1 Progression of lung disease within specific genotypes of patients with cystic fibrosis (CF) – Which lung function parameter differentiates best?

S. Gallati¹, M.H. Schoeni², R. Kraemer³. ¹University of Berne, Division of Human Genetics, Berne, Switzerland; ²University of Berne, Department of Paediatrics, Berne, Switzerland; ³University of Berne, Division of Paediatrics Respiratory Medicine, Berne, Switzerland

Objectives: The relationship between *CFTR* genotypes and functional severity of pulmonary disease in CF has been proven to be difficult to establish. In contrast to previous modelling concepts we stratified genotypes according to the nature of mutations in combination with and without F508del and searched for associations with different lung function parameters (FRC_{pleth}, LCI, V_{TG}, sR_{eff}, FEV₁, FEF₅₀)

Methods: Longitudinal data included repeated measurements of 246 CF patients (124 males; 122 females) aged between 5 and 18 years annually seen between 1987 and 2010. Linear mixed model (LMM) analyses were used to analyse the relationship between each lung function parameter regarding progression with age (slope) and specific genotypes:

A. F508del(2); n=144 vs. F508del_frameshift; n=27 vs. nonF508del_frameshift; n=10

B. F508del(2); n=144 vs. F508del_nonsense; n=27 vs. nonF508del_nonsense; n=11

C. F508del(2); n=144 vs. F508del_missense; n=10 vs. nonF508del_missense; n=9

Results: The degree of bronchial obstruction (sR_{eff}) significantly ($p < 0.01$) decreased with age in nonF508del_frameshift genotypes, ventilation inhomogeneities (LCI) and bronchial obstruction were less pronounced in nonF508del_nonsense groupe, and increase of bronchial obstruction as well as decline in flow limitation (FEV₁, MEF₅₀) were significantly lower in nonF508del_missense patients.

Conclusions: Nature and combination with or without F508del are important stratifying criteria for genotype–phenotype modelling in CF. Extended lung function evaluation is crucial to provide reliable estimate of disease progression and to allow prognostic conclusions.

WS23.2 Chest X-ray scores and chest CT scores up to 5 years apart are highly correlated

D. Sanders¹, Z. Li², J. Collins³, A. Brody⁴, P. Farrell¹. ¹University of Wisconsin, Pediatrics, Madison, United States; ²University of Wisconsin, Biostatistics and Medical Informatics, Madison, United States; ³University of Cincinnati, Radiology, Cincinnati, United States; ⁴Cincinnati Children's Hospital, Radiology, Cincinnati, United States

Background: We recently demonstrated that: (1) the Wisconsin x-ray scoring system (WCXR) is highly sensitive to chest CT abnormalities for chest x-rays obtained within one year of the CT; (2) WCXR scores are strongly predictive of WCXR and FEV₁ severity 5–7 years later. In this study, we hypothesize that WCXR scores obtained up to 5 years before and after a chest CT would be correlated with the Brody CT score.

Methods: In 2000, 81 subjects in the Wisconsin Randomized Control Trial of CF Newborn Screening obtained a high-resolution chest CT at their clinical baseline. Chest x-rays and spirometry were performed annually. The sensitivity, ROC, and correlation between the 2000 Brody CT score and annual WCXR and FEV₁ % predicted obtained between 5 years before and 5 years after the chest CT were calculated.

Results: In 2000, the mean (range) age was 11.6 (6.6–17.6) years. During the 10-year study period, the mean (SD) WCXR worsened from 10.2 (9.6) to 23.4 (14.5); the mean (SD) FEV₁ % predicted remained stable: 91.8 (23.4) in the first year and 92.3 (18.3) in the last year. The correlation between WCXR scores and the CT score ranged from 0.72 to 0.84. In contrast, the correlation between FEV₁ and CT scores ranged from –0.49 to –0.76. The WCXR correlation was statistically significantly better than the FEV₁ correlation in the 4 years before the CT and years 2–4 after.

Conclusion: There is a strong correlation between annual WCXR scores and chest CT score for a period up to 5 years before and 5 years after the CT. Over a 10-year period, longitudinal WCXR scores compare favorably with chest CT and provide more prognostic information on lung disease progression than does FEV₁.

WS23.3 Sputum *Candida albicans* is associated with radiological abnormalities in a cystic fibrosis cohort

T. McEnery¹, S.H. Chotirmall¹, T. Hassan¹, B. McCullagh¹, Z. Abidin¹, S.J. O'Neill¹, C. Gunaratnam¹, M.P. Logan², N.G. McElvaney¹. ¹Beaumont Hospital, Department of Respiratory Medicine, Dublin, Ireland; ²Beaumont Hospital, Department of Radiology, Dublin, Ireland

Introduction: *C. albicans* is commonly isolated from CF sputum and is associated with impaired salivation, diabetes, steroid and antibiotic use. Recent data suggest that the organism presages hospitalized exacerbations and FEV₁ declines [1].

Aim: To determine effect of *C. albicans* colonization on high resolution computed tomography (HRCT) chest imaging in a CF cohort (n=48).

Methods: All patients were evaluated by HRCT and classified according to *C. albicans* colonization status over the preceding 2-year period. Modified bhalla scoring criteria was applied to each scan by a radiologist blinded to colonization status and statistical analysis performed using SPSSv17 software.

Results: Patients colonized with *C. albicans* (n=23) show more severe bronchiectasis ($p < 0.03$) and peribronchial thickening ($p < 0.05$) as compared to those non-colonized (n=25). Significant differences were also detected in the *C. albicans* colonized for the extent of bronchiectasis ($p = 0.025$), mucus plugging ($p = 0.032$), lymphadenopathy ($p = 0.022$) and mosaic pattern ($p = 0.022$). No differences were detected in the presence of sacculations, abscesses, bullae, emphysema, collapse, consolidation or broncholiths.

Conclusion: CF patients colonized by *C. albicans* show more severe radiological abnormalities as compared to those non-colonized. In combination with prior data [1], identification of *C. albicans* should prompt radiological evaluation. Studies assessing the efficacy of therapeutic eradication in CF are now warranted.

Reference(s)

- [1] Chotirmall SH, O'Donoghue E, Bennett K et al. Sputum *Candida albicans* presages FEV₁ decline and hospital-treated exacerbations in cystic fibrosis. Chest 2010 Nov; 138(5): 1186–95.

WS23.4 High Rhinovirus burden in lower airways of children with cystic fibrosis

E. Kieninger¹, F. Singer¹, C. Tapparel², M.P. Alves¹, P. Latzin¹, H.-L. Tan³, C. Bossley³, C. Casaulta³, A. Bush³, J.C. Davies³, L. Kaiser², N. Regamey¹. ¹Division of Paediatric Respiratory Medicine, University Children's Hospital, Inselspital, Bern, Switzerland; ²Laboratory of Virology, Division of Infectious Diseases and Division of Laboratory Medicine, University of Geneva Hospitals and Faculty of Medicine, University of Geneva, Geneva, Switzerland; ³Department of Paediatric Respiratory Medicine, Royal Brompton Hospital, London, United Kingdom

Background: Rhinovirus (RV)-induced pulmonary exacerbations are common in cystic fibrosis (CF) and have been associated with impaired virus clearance by the CF airway epithelium *in vitro*.

Objective: To assess *in vivo* the association of RV prevalence and load with anti-viral defence mechanisms, airway inflammation and lung function parameters in children with CF as compared to children with other chronic respiratory diseases and controls.

Methods: RV presence and load was measured by real-time RT-PCR in bronchoalveolar lavage (BAL) samples and related to anti-viral and inflammatory mediators measured in BAL and to clinical parameters.

Results: BAL samples were obtained from children with CF (n=195), non-CF bronchiectasis (n=40), asthma (n=29) and controls (n=35) at a median (IQR) age of 8.2 (4.0–11.7) years. RV was detected in 73 samples (24.4%). RV prevalence was similar between groups. RV load (median [IQR] $\times 10^3$ copies/mL) was higher in CF (143.0 [13.1–1530.0]), especially during pulmonary exacerbations, compared to asthmatics (3.0 [1.3–25.8], $p = 0.006$) and controls (0.5 [0.3–0.5], $p < 0.001$), but similar to non-CF bronchiectasis (122.1 [2.7–4423.5], $p = \text{NS}$). In children with CF, RV load was negatively associated with IFN- β -1, IL-1 α levels and FEV₁, and positively with IL-8 and IP-10 levels.

Conclusion: RV load in CF BAL is high, especially during exacerbated lung disease. Impaired production of anti-viral mediators, possibly as a consequence of inflammation, may lead to the high RV burden in the lower airways of children with CF.